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Transthoracic Doppler echocardiographic analysis of phasic coronary blood flow velocity in hypertrophic cardiomyopathy

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Abstract

***Objective*—To use transthoracic Doppler echocardiography to assess coronary blood flow non-invasively in patients with hypertrophic cardiomyopathy.**

***Design*—High frequency transthoracic Doppler echocardiography was used to assess resting phasic coronary velocity patterns in patients with hypertrophic cardiomyopathy and to define the relation between coronary flow patterns and clinical, echocardiographic, and haemodynamic manifestations of this condition.**

***Setting*—A tertiary referral cardiothoracic centre.**

***Methods*—Fifteen patients (10 men and five women, mean (SD) age 49 (10·3) years) with asymmetric hypertrophic cardiomyopathy underwent high frequency (5 MHz) transthoracic Doppler echocardiographic assessment of the left anterior descending coronary artery. In addition, standard two dimensional echocardiography was performed. The results were compared with 16 normal participants (nine men and seven women, mean age 61·2 (10·7) years) who had no evidence of cardiac disease.**

***Results*—Biphasic diastolic predominant coronary artery blood velocity profiles were obtained in all patients and controls. Systolic peak blood velocity and velocity time integral were significantly reduced in the hypertrophic cardiomyopathy group compared with controls (11·3 (15·8) cm/s and 1·09 (1·78) cm *v* 20·5 (13·1) cm/s and 4·23 (2·80) cm, respectively, $P < 0·05$). A reversed pattern of systolic blood flow velocity was found in three patients with severe anterior wall and septal hypertrophy. During diastole there was prolongation of the diastolic acceleration (203 (53) ms *v* 110 (60) ms in controls, $P < 0·05$) and deceleration times (487 (200) ms *v* 210 (90) ms in controls, $P < 0·05$). There was no significant difference between those with and without symptoms or a left ventricular outflow tract gradient.**

***Conclusions*—Patients with hypertrophic cardiomyopathy have abnormal systolic and diastolic coronary flow profiles at rest when measured by transthoracic echocardiography.**

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Patients with hypertrophic cardiomyopathy commonly have evidence of myocardial ischaemia despite angiographically normal coronary arteries. Alterations of the coronary circulation have been described in left ventricular hypertrophy and proposed as a mechanism for the development of angina pectoris in these patients. Invasive studies have described a reduced cardiac reserve in patients with left ventricular hypertrophy secondary to many conditions, including aortic stenosis, systemic hypertension, and hypertrophic cardiomyopathy.[1-5] There are few data available on coronary blood flow in unsedated patients with hypertrophic cardiomyopathy. Transthoracic echocardiography allows non-invasive evaluation of coronary flow patterns in the distal segment of the left anterior descending coronary artery (LAD).[6 7] In the present study transthoracic echocardiography was used to assess phasic coronary velocity patterns in patients with hypertrophic cardiomyopathy and to define the relation between coronary flow patterns and clinical and haemodynamic manifestations of this condition.

Methods

PATIENTS

Fifteen patients (10 men and five women, mean (SD) age 49 (10·3) years) admitted to hospital for assessment of hypertrophic cardiomyopathy were studied. The patients were selected from a group of 21 because of the ease of imaging the LAD. Hypertrophic cardiomyopathy was diagnosed on the basis of an echocardiographic demonstration of a hypertrophied and non-dilated left ventricle in the absence of a secondary cause of left ventricular hypertrophy. Thirteen patients had a thickness ratio > 1·5 between the interventricular septum and the posterior wall. Of the remaining two patients, one had evidence of an intraventricular gradient by echocardiography and cardiac catheterisation, and the other had severe hypertrophy without coronary artery disease or hypertension. Eight patients had symptoms of chest pain, palpitation, or dyspnoea. Coronary angiography was performed in 11 patients, all of whom had normal coronary arteries. A control group of 16 normal participants (nine men and seven women, mean age 61·2 (10·7) years) was also studied.

ECHOCARDIOGRAPHY OF THE LAD

Echocardiography of the LAD was performed using a Vingmed CFM 750 ultrasound unit and a 5 MHz mechanical sector transducer.

The transducer has a focal length of 40 mm, with lateral and axial resolutions of 0·6 and more than 0·3 mm, respectively, operating at its nominal frequency. It has a broad band width allowing transmission and reception of ultrasound frequencies over a wide range for imaging and Doppler. A frequency of 6·3 MHz was used for two dimensional imaging and 5 MHz for pulsed Doppler. Images were recorded on super VHS videotape and analysed later by one observer. A careful attempt was made in each patient to visualise the LAD and to obtain a pulsed wave Doppler measurement of blood flow velocity in the vessel.

Detection of the LAD

The echocardiographic technique for assessment of the LAD was as described previously.[8] Patients were examined in the left lateral position using a modified left parasternal window. The transducer was placed in the left parasternal area and the left ventricle imaged in its long axis. The ultrasound beam was angled laterally and superiorly to identify the anterior interventricular sulcus. This area was carefully examined using combined imaging and colour flow mapping. The distal LAD was identified as a tubular structure located within the anterior interventricular sulcus close to the apex with colour flow directed from base to apex and containing characteristic biphasic pulsed Doppler flow signals. Once the position of the LAD was identified intraluminal flow signals were obtained using the pulsed Doppler method. The long axis sections were carefully adjusted to minimise the angle between the Doppler beam and the long axis of the artery and to ensure that the sampling volume was located within the vessel lumen for as much of the cardiac cycle as possible. The Doppler signal and two dimensional echocardiogram were then recorded.

Doppler velocity measurements

Velocity measurements were performed using the internal analysis package of the ultrasound unit. Measurements were calculated taking into consideration the angle between the Doppler beam and the longitudinal axis of the blood vessel as determined by the two dimensional echocardiogram. Absolute velocity was reported as the product of the measured velocity and the cosine of the angle between the Doppler beam and the direction of blood flow. Seven variables were measured by tracing the contour of the Doppler velocity pattern: peak systolic velocity; peak diastolic velocity; systolic velocity time integral; diastolic velocity time integral; diastolic acceleration time, defined as the time from onset of diastolic flow to attainment of peak velocity; diastolic deceleration time, defined as the time from attainment of peak diastolic flow velocity to the cessation of flow; and time from the beginning of the Q wave on the electrocardiogram to the start of diastolic blood flow. Values for each variable were obtained by averaging measurements from five to seven consecutive cardiac cycles. We have reported previously that measurement of coronary flow velocity profiles by this method is reproducible with satisfactory interobserver and intraobserver variability.[9]

OTHER ECHOCARDIOGRAPHIC MEASUREMENTS

Standard M mode, two dimensional, and Doppler transthoracic echocardiography were also performed with a Hewlett Packard Sonos 1500 ultrasound machine using a 2·5 MHz transducer. Cardiac dimensions were measured according to previously described techniques.[10 11] Left ventricular wall thickness was determined by the end diastolic ventricular septal thickness at the chordal and papillary muscle levels.

STATISTICAL ANALYSIS

Results are presented as means (SD). Data were analysed using the unpaired Student's t test. A P value $< 0·05$ was considered significant. A best-fit linear regression equation was calculated using the least squares method and a correlation coefficient was obtained.

Results

PATIENT CHARACTERISTICS

Table 1 shows patient characteristics. All patients with hypertrophic cardiomyopathy had significant thickening of the left ventricular septum compared with that of the control group (2·7 (0·5) cm v 0·8 (0·2) cm, $P < 0·01$).

Table 1 Patient characteristics

Patient (sex)	Age (years)	Symptoms	Coronary angiography	LVOT gradient (mm Hg)	Left ventricular wall thickness measurements			
					AWT (cm)	PWT (cm)	ST (cm)	ST/PWT (cm)
1 (F)	65	+	+	120	2·21	0·96	2·65	2·76
2 (F)	50	+	+	110	1·78	1·53	2·33	1·52
3 (F)	50	+	+	120	1·78	0·93	1·62	1·52
4 (F)	45	+	+	80	1·28	1·50	1·90	1·27
5 (M)	56	—	—	0	2·90	1·20	2·80	2·33
6 (M)	46	—	+	0	2·49	1·38	2·68	1·942
7 (M)	33	+	+	0	2·85	0·91	3·17	3·52
8 (M)	65	—	+	0	2·82	2·51	2·7	1·08
9 (M)	58	+	+	0	3·20	1·40	3·61	2·60
10 (M)	27	—	+	0	2·80	1·75	3·20	1·83
11 (M)	49	+	—	15	1·29	1·32	3·01	2·28
12 (M)	48	—	+	140	1·71	1·2	2·33	1·94
13 (F)	52	+	—	95	2·50	1·10	2·70	2·46
14 (M)	58	—	+	0	2·70	1·50	3·04	2·00
15 (M)	46	—	+	0	2·70	1·60	3·02	1·88

AWT, anterior wall thickness; LVOT, left ventricular outflow tract; PWT, posterior wall thickness; ST, septal thickness.

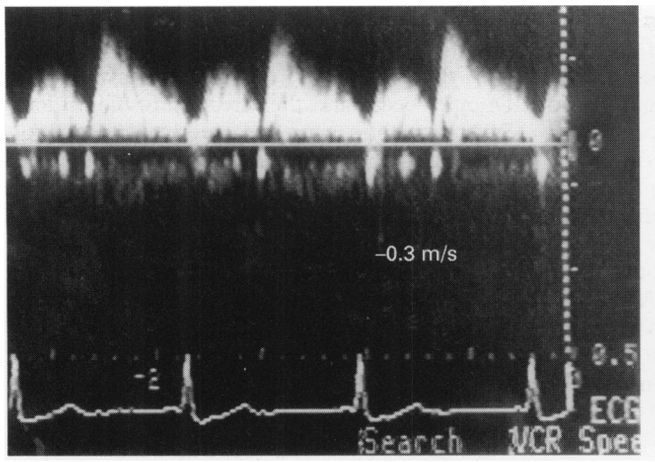

Figure 1 Normal blood velocity profile in the left anterior descending coronary artery. Blood flow is biphasic and predominant during diastole. Forward flow occurs during systole and diastole.

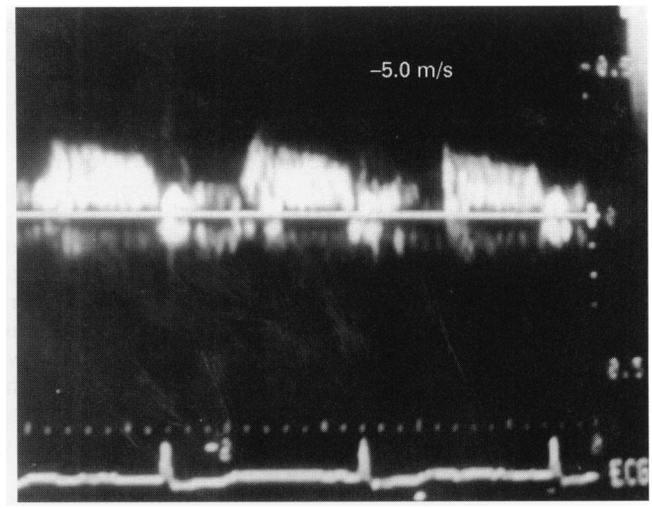

Figure 2 Blood velocity profile from a patient with hypertrophic cardiomyopathy. Velocity is significantly diminished during systole. During diastole the acceleration and deceleration times are prolonged.

The ventricular/posterior wall thickness ratio was 2·0 (0·7) in the hypertrophic cardiomyopathy group compared with 1·0 (0·1) in the controls. Evidence of an intraventricular gradient by Doppler echocardiography was present in seven patients and was ⩾ 80 mm Hg in six.

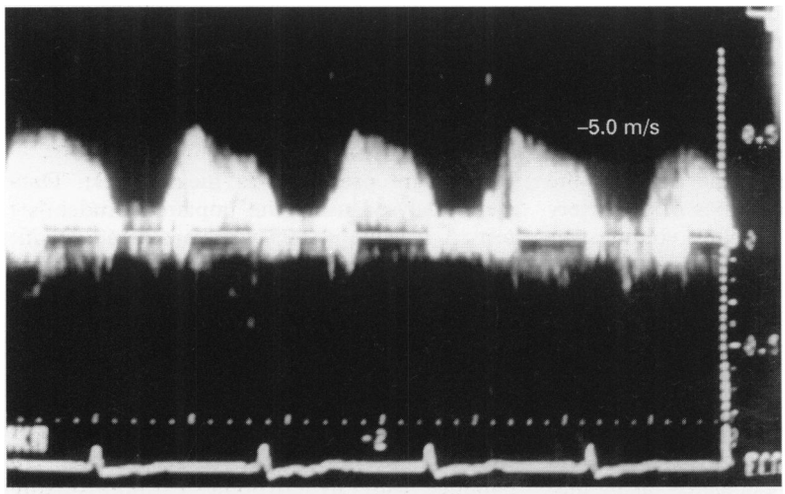

Figure 3 Blood velocity pattern from a patient with hypertrophic cardiomyopathy. No blood flow velocity pattern is present during systole.

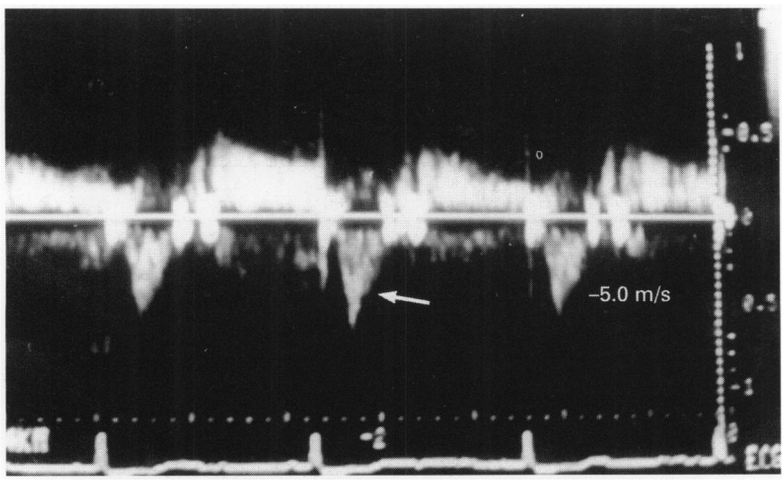

Figure 4 Blood velocity profile from a patient with hypertrophic cardiomyopathy. Reversed blood flow (arrow) occurs during systole.

ECHOCARDIOGRAPHIC DATA

The distal LAD appeared to be normal at the site of measurement in all patients and controls. High quality Doppler spectral traces were obtained. The mean incident angle between the Doppler beam and blood flow was 42° (4·1°) in the patients and 46° (6·2°) in the controls. Biphasic blood velocity profiles corresponding to systole and diastole were observed in all patients and controls. Blood flow velocity was predominant during diastole (fig 1).

Systolic peak blood velocity and velocity time integral were significantly reduced in the hypertrophic cardiomyopathy group compared with that in the controls (11·3 (15·8) cm/s and 1·09 (1·78) cm *v* 20·5 (13·1) cm/s and 4·23 (2·80) cm, respectively, $P < 0·05$) (figs 2 and 3). A reversed pattern of systolic blood flow was found in three patients with severe anterior wall and septal hypertrophy (table 2 and fig 4).

There was no significant difference in diastolic peak velocity or velocity time integrals between the controls and patients with hypertrophic cardiomyopathy (table 3). Morphology of the diastolic velocity profile was abnormal, however, in patients with hypertrophic cardiomyopathy. There was a slow upstroke caused by prolongation of the acceleration time (203 (53) ms *v* 110 (60) ms in controls, $P < 0·05$) and a slow downstroke at the end of diastole causing a prolonged deceleration time (487 (200) ms *v* 210 (90) ms in controls, $P < 0·05$).

COMPARISON OF PATIENT SUBGROUPS

In the hypertrophic cardiomyopathy group there was no significant difference in any of the systolic or diastolic values between those with and without symptoms or an intraventricular gradient. There was no significant correlation between measurements of systolic or diastolic

Table 2 Coronary haemodynamic data

Patient (sex)	HR (beats/min)	Ps (cm/s)	Pd (cm/s)	VTIs (cm)	VTId (cm)	AT (ms)	DT (ms)
1 (F)	68	−11	24	−1·62	8·87	180	380
2 (F)	66	20	37	2·41	12·53	120	310
3 (F)	71	−17	32	−2·69	9·98	160	220
4 (F)	83	10	45	1·82	16·95	330	220
5 (M)	69	51	51	4·50	21·47	170	450
6 (M)	52	14	36	2·80	15·70	230	350
7 (M)	48	8	33	1·23	19·95	280	740
8 (M)	57	−7	46	−0·97	21·37	200	660
9 (M)	68	14	25	0·45	11·34	180	720
10 (M)	56	12	52	2·03	15·10	170	420
11 (M)	57	10	43	1·62	19·54	230	410
12 (M)	81	8	74	1·22	23·21	230	290
13 (F)	62	20	46	1·23	20·43	180	700
14 (M)	75	17	32	1·30	15·21	160	680
15 (M)	69	21	41	0·94	19·13	230	760

AT, acceleration time; DT, deceleration time; HR, heart rate; Pd, diastolic peak velocity; Ps, systolic peak velocity; VTId, diastolic velocity time integral; VTIs, systolic velocity time integral.

velocity and the severity of the intraventricular gradient or between systolic peak velocity and septal thickness.

Discussion

In this study a non-invasive echocardiographic technique was used to assess coronary blood velocity patterns in patients with hypertrophic cardiomyopathy. Patients with this condition had reduced or reversed systolic peak blood velocity and velocity time integral compared with that of the controls. There was no overall effect on peak velocity during diastole but the velocity profile was broadened showing a slower upstroke to peak velocity and also a slower downstroke back to baseline at the end of diastole. There were no significant differences between those with and without symptoms or a left ventricular outflow tract gradient.

Hypertrophic cardiomyopathy in the presence of angiographically normal coronary arteries is frequently accompanied by clinical and histological findings suggestive of myocardial ischaemia regardless of the presence or absence of left ventricular outflow tract obstruction.[12-14] Evidence has been found of impaired regional left ventricular function at rest by echocardiography and of reversible exercise induced defects in myocardial perfusion by thallium-201 imaging.[15 16] Postmortem examination has shown myocardial fibrosis, left ventricular necrosis, and transmural scarring.[12 17]

Abnormalities in coronary flow dynamics, in the absence of coronary artery stenosis, have been proposed as a mechanism for the development of myocardial ischaemia in patients with hypertrophic cardiomyopathy. A reduction in coronary reserve has been reported in most studies,[4 18 19] a finding that also occurs in other causes of left ventricular hypertrophy, such as aortic stenosis, systemic hypertension, and aortic regurgitation.[2 4 20 21] The reduction in coronary reserve in patients with hypertrophic cardiomyopathy has been attributed to a decrease in myocardial capillary density relative to the increase in myocardial mass.[4 22] These changes lead to a reduced vasodilator reserve when calculated on the basis of flow per gram of myocardial tissue. Other anatomical and haemodynamic abnormalities that may contribute to the development of ischaemia include regional deficiencies in myocardial flow and flow reserve as demonstrated by perfusion defects during stress exercise; luminal narrowing of small vessels; intimal hyperplasia; and systolic compression of the septal perforator arteries.[4 23 25] These coronary vascular abnormalities may affect coronary reserve and resting blood flow.

There are few data available on phasic coronary flow dynamics in hypertrophic cardiomyopathy. Memmola *et al*[19] measured coronary reserve in the proximal LAD of 10 patients with obstructive hypertrophic cardiomyopathy by transoesophageal echocardiography. All patients were symptomatic and had an intraventricular pressure gradient. Systolic flow was reduced and reversed flow occurred in three patients. Coronary flow reserve was inversely correlated with the baseline intraventricular gradient. The results of our study extend these observations to a larger group of patients with hypertrophic cardiomyopathy. There was no significant difference between patients with or without symptoms or an outflow tract gradient. Abnormalities of systolic and diastolic flow were found in both groups compared with normal controls. There was no relation between phasic flow abnormalities and those with symptoms or an outflow tract gradient.

Most blood flow in normal coronary arteries occurs during diastole as myocardial compression during systole increases distal vascular resistance.[26 27] This biphasic diastolic predominant blood velocity pattern was found in all controls and patients with hypertrophic cardiomyopathy. The reduction and reversal in systolic flow velocity and alterations in the

Table 3 Summarised coronary haemodynamic data in patients and controls

	Controls	Patients	P value
HR (beats/min)	65·5 (13·6)	65·5 (10·0)	NS
Ps (cm/s)	20·5 (13·1)	11·3 (15·8)	< 0·05
Pd (cm/s)	39·7 (20·5)	41·1 (12·5)	NS
VTIs (cm)	4·23 (2·80)	1·09 (1·78)	< 0·05
VTId (cm)	14·16 (7·89)	16·72 (4·50)	NS
AT (ms)	110 (60)	203 (53)	< 0·05
DT (ms)	210 (90)	487 (200)	< 0·05
TD (ms)	124 (51)	443 (107)	< 0·05

Values are mean (SD) where appropriate.
AT, acceleration time; DT, deceleration time; HR, heart rate; Pd, diastolic peak velocity; Ps, systolic peak velocity; TD, time from the beginning of the Q wave on the electrocardiogram to the onset of diastolic flow; VTId, diastolic velocity time integral; VTIs, systolic velocity time integral.

diastolic velocity pattern in the hypertrophic cardiomyopathy group may be a result of several contributory factors. Firstly, the abnormally increased intramyocardial pressure that occurs during systole may lead to increased coronary arterial resistance. Reversed blood flow in the normal heart occurs during systole in intramural coronary arteries probably because of the high extravascular pressure generated during cardiac contraction.[28] Animal studies have reported exaggeration of this reversed systolic flow velocity by increasing the extravascular pressure.[28] Systolic compression of large intramural vessels or abnormally narrowed small intramural coronary arteries in patients with hypertrophic cardiomyopathy may produce functionally important increases in coronary vascular resistance, leading to augmented backward flow into the epicardial arteries.[24 25]

Secondly, it has been postulated that the epicardial arteries act as capacitance vessels.[26 29] Under normal conditions these vessels are very compliant, two to three times that of similarly sized systemic arteries. They can undergo up to a 5% change in diameter over the cardiac cycle.[30 31] The epicardial arteries in patients with hypertrophic cardiomyopathy are dilated so the maximum capacitance effect may be reduced.[32] This would cause a reduction in the "charging" effect during systole, which would in turn cause a reduction in "discharging" of blood from the vessel during diastole. This mechanism may also contribute to the abnormal flow patterns observed during systole and diastole in this study.

Thirdly, left ventricular diastolic dysfunction is a common finding in patients with hypertrophic cardiomyopathy.[33] Coronary blood velocity patterns may be affected by prolonged asynchronous relaxation due to myocardial fibre disarray.[34 35]

All these abnormalities may be present in patients with hypertrophic cardiomyopathy regardless of the presence or absence of a left ventricular outflow tract gradient and may explain in part the lack of a correlation between abnormal phasic coronary velocities and outflow tract obstruction. Blood velocity patterns at rest have also been found in patients with hypertrophy due to aortic stenosis and hypertension. It has been reported that reversed systolic flow in patients with hypertrophy due to aortic stenosis normalised within one week after aortic valve replacement without significant change in the degree of hypertrophy.[5 21] By contrast, systolic and diastolic peak velocities were increased in patients with hypertrophy due to hypertension.[36] This suggests that different mechanisms may affect blood velocity profiles depending on the cause of ventricular hypertrophy.

LIMITATIONS

The echocardiographic technique described here allows non-invasive assessment of phasic blood velocity profiles. The methods has satisfactory interobserver and intraobserver variability.[9] However, it allows assessment of blood flow only in the LAD. Therefore regional differences in coronary flow in patients with non-uniform myocardial abnormalities, such as coronary artery disease or hypertrophic cardiomyopathy, cannot be compared.

Echocardiographic detection of the LAD is variable (30–80%).[6 37] It is easier in patients with good acoustic windows and left ventricular hypertrophy. Use of this technique in selected populations may improve the detection rate. Developments in echocardiography, such as the use of echo-contrast agents capable of enhancing Doppler signal intensity after intravenous injection, may increase the clinical applicability of this technique.[38] When using Doppler, the incident angle between the Doppler beam and the direction of flow may be large. We measured only those signals which provided distinct velocity envelopes during systole and diastole. These are known to lead to reproducible velocity profiles in other vessels.[39 40]

Conclusions

A non-invasive Doppler echocardiographic technique was used to characterise phasic coronary blood flow in patients with hypertrophic cardiomyopathy under physiological conditions. Systolic coronary flow velocities were significantly reduced and there was reversal of systolic flow in three patients. During diastole the rates of acceleration and deceleration of diastolic flow were prolonged. Further studies may allow assessment of the effects of drug treatment or other interventions on the haemodynamics of coronary flow in this condition.

1 Houghton JL, Frank MJ, Carr AA, Von Dohlen TW, Prisant M. Relations among impaired coronary flow reserve, left ventricular hypertrophy and thallium perfusion defects in hypertensive patients without obstructive coronary artery disease. *J Am Coll Cardiol* 1990;**15**: 43–51.

2 Opherk D, Mall G, Zebe H, Schwarz F, Weihe E, Manthey J, *et al.* Reduction of coronary reserve: a mechanism for angina pectoris in patients with arterial hypertension and normal coronary arteries. *Circulation* 1984;**69**:1–7.

3 Camici P, Chiriatti G, Lorenzoni R, Bellina RC, Gistri R, Italiani G, *et al.* Coronary vasodilation is impaired in both hypertrophied and nonhypertrophied myocardium of patients with hypertrophic cardiomyopathy: a study with nitrogen-13 ammonia and positron emission tomography. *J Am Coll Cardiol* 1991;**17**:879–86.

4 Cannon ROI, Rosing DR, Maron BJ, Leon MB, Bonow RO, Watson RM, *et al.* Myocardial ischemia in patients with hypertrophic cardiomyopathy: contribution of inadequate vasodilator reserve and elevated left ventricular filling pressures. *Circulation* 1985;**71**:234–43.

5 Kenny A, Wisbey CR, Shapiro LM. Profiles of coronary blood flow velocity in patients with aortic stenosis and the effect of valve replacement: a transthoracic echocardiographic study. *Br Heart J* 1994;**71**:57–62.

6 Kenny A, Shapiro LM. Transthoracic high-frequency two-dimensional echocardiography, Doppler and color flow mapping to determine anatomy and blood flow patterns in the distal left anterior descending coronary artery. *Am J Cardiol* 1992;**69**:1265–8.

7 Miyatake K, Yamagishi M, Izumi S, Beppu S, Yamamoto K, Sakakibara H, *et al.* Doppler echocardiographic approach to the blood flow of the left anterior descending coronary artery. *J Clin Ultrasound* 1988;**16**:471–81.

8 Crowley JJ, Shapiro LM. Noninvasive assessment of left internal mammary artery graft patency using transthoracic echocardiography. *Circulation* 1995;**92**:II-25–30.

9 Kenny A, Wisbey CR, Shapiro LM. Measurement of left anterior descending coronary artery flow velocities by transthoracic Doppler ultrasound. *Am J Cardiol* 1994;**73**: 1021–2.

10 Gilbert BW, Pollick C, Adelman AG, Wigle D. Hypertrophic cardiomyopathy: subclassification by M mode echocardiography. *Am J Cardiol* 1980;**45**:861–72.

11 Abbasi AS, MacAlpin RN, Eber LM, Pearce ML. Echocardiographic diagnosis of idiopathic hypertrophic

cardiomyopathy without outflow obstruction. *Circulation* 1972;**46**:897–904.
12 Tanaka M, Fujiwara H, Onodera T, Wu D-J, Hamashima Y, Kawai C. Quantitative analysis of myocardial fibrosis in normals, hypertensive hearts, and hypertrophic cardiomyopathy. *Br Heart J* 1986;**55**:575–81.
13 Maron BJ, Bonow RO, Cannon RO, Leon MB, Epstein SE. Hypertrophic cardiomyopathy: interrelation of clinical manifestations, pathophysiology and therapy. Part 1. *N Engl J Med* 1987;**316**:780–9.
14 Maron BJ, Epstein SE, Roberts WC. Hypertrophic cardiomyopathy and transmural myocardial infarction without significant atherosclerosis of the extramural coronary arteries. *Am J Cardiol* 1979;**43**:1086–102.
15 St John Sutton MG, Tajik AJ, Smith HC, Ritman EL. Angina in idiopathic hypertrophic subaortic stenosis: a clinical correlate of regional left ventricular dysfunction: a videometric and echocardiographic study. *Circulation* 1980;**54**:484–94.
16 Pitcher D, Wainwright R, Maisey M, Curry P, Sowton E. Assessment of chest pain in hypertrophic cardiomyopathy using exercise thallium-201 myocardial scintigraphy. *Br Heart J* 1980;**44**:650–6.
17 St John Sutton MG, Lie JT, Anderson KR, O'Brien PC, Frye RL. Histopathological specificity of hypertrophic obstructive cardiomyopathy: myocardial fibre disarray and myocardial fibrosis. *Br Heart J* 1980;**44**:433–43.
18 Akasaka T, Yoshikawa J, Yoshida K, Maeda K, Takagi T, Miyake S. Phasic coronary flow characteristics in patients with hypertrophic cardiomyopathy: a study by coronary Doppler catheter. *J Am Soc Echocardiogr* 1994;7:9–19.
19 Memmola C, Illiceto S, Napoli VF, Cavallari D, Santoro G, Rizzon P. Coronary flow dynamics and reserve assessed by transesophageal echocardiography in obstructive hypertrophic cardiomyopathy. *Am J Cardiol* 1994;**74**:1147–51.
20 Pichard AD, Gorlin R, Smith H, Ambrose J, Meller J. Coronary flow studies in patients with left ventricular hypertrophy of the hypertensive type. *Am J Cardiol* 1981;**47**:547–54.
21 Hongo M, Goto T, Watanabe N, Nakatsuka T, Tanaka M, Kinoshita O, *et al*. Relation of phasic coronary flow velocity profile to clinical and hemodynamic characteristics of patients with aortic valve disease. *Circulation* 1993;**88**:953–60.
22 Pasternac A, Noble J, Streulens Y, Elie R, Henschke C, Bourassa MG. Pathophysiology of chest pain in patients with cardiomyopathies and normal coronary arteries. *Circulation* 1982;**65**:778–89.
23 Hanrath P, Mathey R, Montz R, Thiel U, Vorbringer H, Kupper W, *et al*. Myocardial thallium-201 imaging in hypertrophic obstructive cardiomyopathy. *Eur Heart J* 1981;**2**:177–85.
24 Maron BJ, Wolfson JK, Epstein SE, Roberts WC. Intramural ("small vessel") coronary artery disease in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1986; **8**:545–57.
25 Pichard AD, Meller J, Teicholz LE, Lipnik S, Gorlin R, Herman MV. Septal perforator compression (narrowing) in idiopathic hypertrophic subaortic stenosis. *Am J Cardiol* 1977;**40**:310–4.
26 Spaan JAAE, Breuls NPW, Laird JD. Diastolic-systolic coronary flow differences are caused by intramyocardial pump action in the anesthetized dog. *Circ Res* 1981; **49**:584–93.
27 Segal J. Applications of coronary flow velocity during angioplasty and other coronary interventional procedures. *Am J Cardiol* 1993;**71**:17–25D.
28 Chilian WM, Marcus ML. Effects of coronary and extravascular pressure on intramyocardial and epicardial blood velocity. *Am J Physiol* 1985;**248**:H170–8.
29 Chilian WM, Marcus ML. Phasic coronary flow velocity in intramural and epicardial arteries. *Circ Res* 1982;**50**: 775–81.
30 Tomoike H, Ootsubo H, Sakai K, Kikuchi Y, Nakamura M. Continuous measurement of coronary artery diameter in situ. *Am J Physiol* 1981;**240**:H73–9.
31 Vatner SF, Pagani M, Manders WT, Pasipoularides AD. Alpha adrenergic vasoconstriction and nitroglycerin vasodilation of large coronary arteries in the conscious dog. *J Clin Invest* 1980;**65**:5–14.
32 Kimball BP, LiPreti V, Bui S, Wigle ED. Comparison of proximal left anterior descending and circumflex coronary artery dimensions in aortic valve stenosis and hypertrophic cardiomyopathy. *Am J Cardiol* 1990;**65**:767–71.
33 Maron BJ, Spirito P, Green KJ, Wesley YE, Bonow RO, Arce J. Noninvasive assessment of left ventricular function by pulsed Doppler echocardiography in patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1987; **10**:733–42.
34 Wigle ED. Hypertrophic cardiomyopathy: a 1987 viewpoint. *Circulation* 1987;**75**:311–22.
35 Maron BJ, Bonow RO, Cannon RO, Leon MB, Epstein SE. Hypertrophic cardiomyopathy: interrelation of clinical manifestations, pathophysiology and therapy. Part 2. *N Engl J Med* 1987;**316**:844–52.
36 Isaaz K, Bruntz JF, Paris D, Ethevenot F, Aliot E. Abnormal coronary flow velocity pattern in patients with left ventricular hypertrophy, angina pectoris, and normal coronary arteries: a transesophageal Doppler echocardiographic study. *Am Heart J* 1994;**128**:500–10.
37 Ross JJ, Ren J, Land W, Chandrasekaran K, Mintz GS. Transthoracic high frequency (7·5 MHz) echocardiographic assessment of coronary vascular reserve and its relation to left ventricular mass. *J Am Coll Cardiol* 1990; **16**:1393–7.
38 Illiceto S, Caiati C, Aragona P, Verde R, Schlief R, Rizzon P. Improved Doppler signal intensity in coronary arteries after intravenous peripheral injection of a lung crossing contrast agent (SHU 508 A). *J Am Coll Cardiol* 1994; **23**:184–90.
39 Hatle L. Noninvasive assessment and differentiation of left ventricular outflow obstruction with Doppler ultrasound. *Circulation* 1981;**64**:381–7.
40 Lewis BD, James EM, Welch TJ. Current applications of duplex and color Doppler ultrasound imaging: carotid and peripheral vascular system. *Mayo Clin Proc* 1989; **64**:1147–57.